of the antigenic structure of the parasite, with large numbers of different epitopes that are, in part, stage-specific and, furthermore, may vary between strains. Adjuvants also influence the type of immune response. The growing knowledge of pathogenesis, and host-dependent genetic and immunologic factors involved in the clinical outcome of *P. falciparum* malaria, and the insight into the parasite's evasion mechanisms, help us to understand the interactions of this infectious agent with the host's immune system. We now believe that malaria vaccines will eventually be available. We do not, however, believe that vaccines alone will lead to the eradication of this disease.

S162 The future of global strategies for vaccination: WHO perspectives

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Future vaccination strategies will certainly be related to the potential impact of vaccination on morbidity and mortality directly or indirectly associated with specific infectious diseases. About 1.8 million children die of infection in the neonatal period (0–4 weeks of age), particularly in Asia and Africa. The main causes of death are bacterial infections caused by *Staphylococcus aureus*, group A streptococci, *Streptococcus pneumoniae*, Gram-negative coliforms and *Salmonella* as well as neonatal tetanus. During the post-neonatal period (1–12 months), severe infant infections are responsible for over 2 million deaths. In the developing world, the major causes are acute respiratory infections due to pneumococci, *Haemophilus influenzae* or pertussis as well as diarrhea caused by rotavirus, shigella, *Salmonella* or *E. coli*. This contrasts with the greater importance of respiratory viruses (RSV, parainfluenza and influenza), urinary infections, and rotavirus diarrhea in industrialized countries. Although a number of new vaccines are now becoming available to meet this challenge, vaccination strategies to prevent early-life infectious diseases should be selected and adapted accordingly. They will include maternal immunization for early neonatal infections, as well as vaccination in early infancy (0–3 months) for early-occurring diseases. Problems to be solved are mainly related (1) to safety issues (maternal or neonatal immunization), (2) to immunologic immaturity and T-cell polarization (0–3 months immunization), (3) to the duration of induced protection and memory, and (4) to inhibition of infant responses by maternal antibodies.

Recent developments in cardiovascular infections

S163 Do we still need prophylaxis against infective endocarditis?

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The answer is yes, even according to a recent population-based, case-control study from Philadelphia, USA (Ann Intern Med 1998;129: 761–9) challenging the current recommendations for prophylaxis for infective endocarditis (IE). The findings indicate that dental treatment is not a risk factor. However, differences in dental health, dental status and dental care between case patients and controls were not considered. This study will not change our attitude towards the necessity for antimicrobial prophylaxis, but underlines the need for data regarding the correlation between the magnitude of bacteremia (CFU/mL blood) in connection with dental procedures and the incidence of IE. It is likely that prophylaxis should be downgraded to 'not recommended' for some dental procedures. Since oral microorganisms are still responsible for most cases of IE, it is obvious that prevention should be upgraded, with maintenance of better dental care in patients at risk for IE. Prophylaxis in children, especially with major congenital heart conditions, requires further investigation and discussions. Prevention of nosocomial endocarditis represents a formidable clinical challenge, with the introduction of new cardiac devices like implantable cardiovascular defibrillators and left ventricular assist devices, raising questions of hardware removal in cases of infection or chronic suppressive antimicrobial therapy. The incidence and mortality of prosthetic valve endocarditis are still unacceptably high. Here also we should focus on prevention (surgical techniques, surgical materials, treatment of perioperative bacteremias, dental health) rather than efforts to amplify antimicrobial prophylaxis.

S164 New antibiotic treatment modalities

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Treatment of *Staphylococcus aureus* and streptococcal endocarditis requires prolonged administration of parenteral β-lactams or vancomycin. Newer quinolones are active against Gram-positive bacteria, are well absorbed after oral administration, and have a prolonged serum $t1/2$, allowing once-daily dosage. Levofloxacin, trovafloxacin and moxifloxacin were tested in rats with *S. aureus* or streptococcal experimental endocarditis (EE). They were compared to ciprofloxacin (Cipro) and vancomycin (Vanco) for *S. aureus*, or ceftriaxone for streptococci. The risk of resistance selection was examined. Against Cipro-susceptible *S. aureus*, all three new quinolones were equivalent or more active than Cipro and Vanco in vitro and in vivo, and were markedly less prone than Cipro to select for quinolone resistance. However, they were ineffective against *S. aureus* already resistant to Cipro. Two experimental quinolones (Y-688 and S-34109) with high in vitro activity against Cipro-resistant *S. aureus* also failed in rats, and selected for mutants with increased MICs. Thus, once resistant to Cipro, *S. aureus* may easily acquire additional mutations, making it resistant to the most powerful quinolones. Against streptococci, levofloxacin was effective against EE due to penicillin-susceptible and -resistant isolates. In contrast, trovafloxacin failed in similar experiments. Time-kill experiments indicated that very low concentrations (×2 and ×4 MIC) of levofloxacin were more bactericidal than trovafloxacin against streptococci, suggesting that higher doses of this drug should be used in this situation. This was not observed for *S. aureus*. We conclude that newer quinolones might be convenient and effective against Cipro-susceptible (but not -resistant) *S. aureus* and streptococcal infections. Moreover, they are less prone than older quinolones to select for resistance.

S165 Anti-infective impregnation of vascular prostheses and cardiac prosthetic valves: rationale and experimental evidence

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Anti-infective agents have been bound to a variety of implantable or indwelling medical devices in an attempt to increase local concentrations of antimicrobial or antiseptic agents and to reduce the risk of foreign body infections. This approach has been shown to be successful in some clinical settings (such as silver-coated intravascular catheters) but unsuccessful in others. For the prevention or treatment

of vascular graft infections, a variety of anti-infectives bound to graft materials have been studied in vitro and under experimental in vivo conditions. Of these, gelatin-sealed Dacron grafts containing bound rifampin appear to have the most favorable pharmacokinetics in vitro. Experimental models demonstrate efficacy for the prevention of infection following contamination of the graft either directly or hematogenously, as well as efficacy for the treatment of established infection when rifampin-containing grafts are used as part of surgical therapy. To date, however, results reported from two randomized clinical trials involving over 3100 patients have not shown a statistically significant reduction in graft infections.

Both the incidence of endocarditis and the mortality among patients with endocarditis are higher among patients with cardiac prosthetic valves than among patients with native cardiac valves. Endocarditis affecting prosthetic cardiac valves typically originates in the sewing ring. Recently, St Jude prosthetic cardiac valves using Dacron sewing rings impregnated with silver (Silzone) have been introduced into clinical practice. In vitro, Silzone inhibits attachment and growth of microorganisms. A large, international randomized clinical trial designed to determine whether Silzone is effective in reducing the incidence of prosthetic valve endocarditis is in progress.

S166 Medical versus surgical therapy in native and prosthetic valve endocarditis

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Infective endocarditis (IE) of native and prosthethic heart valves is still burdened by a high mortality. While cumulative survival in uncomplicated IE is 0.93±0.05, manifestation of any of the typical complications (e.g. congestive heart failure, thromboembolism, persistent sepsis, acute renal failure), vegetation size 10 mm, culture-negative endocarditis and a delay in diagnostic decision-making has a significant negative prognostic influence. Early surgical intervention has significantly contributed to the overall prognostic improvement during the last two decades. Evidence-based experience with more than 600 consecutive patients with acute IE has been used to establish criteria to determine which patients may benefit from urgent surgical intervention: acute aortic regurgitation with lung edema not compensated medically within 24 h; acute mitral regurgitation with lung edema not compensated by PEEP; ventilation and modulation of the left ventricular impedance by sufficient afterload reduction; thromboembolic complications (TE) within 30 days after manifestation of IE, if residual vegetations are demonstrated post-TE; recurrent thromboembolic episodes; vegetations larger than 10 mm in mitral IE; demonstration of secondary mitral valve involvement in aortic IE; sepsis persisting for more than 48 h despite antimicrobial therapy; acute renal failure of any etiology; large vegetation size (VS) and a high minimal bactericidal concentration (MBC). Medical cure rates are low and the risk of complications is high if VS is 10 mm and MBC is 1 mg/L.

Current aspects in anaerobic infections

S168 Antimicrobial resistance in anaerobic bacteria

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Human pathogenic anaerobic bacteria were susceptible until a few years ago to antimicrobial agents used in prophylaxis and treatment of anaerobic infections. However, during recent years resistance to certain anti-anaerobic drugs has been reported more frequently from different parts of the world. The Etest method (more reliable than the disk diffusion method) has become available for routine laboratories to evaluate the resistance of clinical isolates to most widely used antibiotics. Antibiotic resistance due to beta-lactamase activity is observed most frequently among *Bacteroides fragilis* group strains; however, more and more *Prevotella, Porphyromonas* and *Fusobacterium* strains have been reported to be resistant to different antimicrobial agents. The metallo-beta-lactamase production of *B. fragilis* is responsible for the resistance to carbapenems. The presence of the *cfiA* gene, coding for this enzyme, has been detected by PCR among carbapenem-susceptible strains in different parts of Europe. Decreased permeability and modification of the PBPs has also been reported as the cause of resistance to cefoxitin, ureidopenicillins and inhibitor combinations. Clindamycin resistance among clinically important anaerobes varies in different parts of the world. Among Gram-negative anaerobes, a low number of strains resistant to metronidazole have also been detected in different countries. According to the in vitro data, the newest fluoroquinolones, such as trovafloxacin, clinafloxacin and grepafloxacin, have considerable anti-anaerobic activity.

S169 Current aspects of anaerobic infections

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The normal human microflora contains both aerobic and anaerobic bacteria. The human gastric mucosa is colonized by the indigenous bacteria in low numbers in healthy persons due to the low pH of the stomach. The bacteria are also protected from the gastric acid by the mucosal layer in the stomach. Impaired gastric secretion causes proliferation of acid-tolerant streptococci and lactobacilli. When the pH is constantly over 4, proliferation of other anaerobic bacteria such as bacteroides and fusobacteria can occur. These bacteria colonize the mucosa without any signs of mucosal inflammation, in contrast to *Helicobacter pylori*. It is now accepted that the finding of *Helicobacter pylori* is associated with gastritis and peptic ulcer disease. Treatments for *Helicobacter pylori* infections include proton pump inhibitors in combination with antimicrobial agents with different clinical responses. Probiotics containing anaerobic bacteria have also been reported to be successful in the treatment of these infections. In patients treated with a proton pump inhibitor, anaerobic bacteria such as veillonellae, bacteroides and fusobacteria are increased when *Helicobacter pylori* is significantly decreased. Patients receiving a proton pump inhibitor together with antimicrobial agents have also increased numbers of anaerobic bacteria when *Helicobacter pylori* is eradicated from the gastric microflora. Thus, there is an inverse relationship between the anaerobic microflora and *Helicobacter pylori* during proton pump inhibitor/antimicrobial treatment.